

## **REMARKS**

### **Status of the Claims**

Claims 1-7, 9-11, 15-19, and 24-26 are currently pending and under examination. Claims 8, 12-14 and 20-23 have been canceled without prejudice or disclaimer of the subject matter claimed therein.

### **Rejection under 35 U.S.C. § 112, first paragraph**

Claims 1-11 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Office Action alleges that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey that at the time the application was filed that the inventor was in possession of the claimed invention.

The present invention provides a method for determining whether an agent modulates a preselected biological condition controlled by the circadian clock. Claim 8 has been canceled without prejudice or disclaimer of the subject matter claimed therein.

The Office Action rejected claims 1-11 on the basis that the specification does not define adequately what an “agent” is. The claimed invention is directed to a method for identifying an agent that modulates a preselected condition controlled by the circadian clock. The claimed invention is not directed to the agents themselves, but to a process that enables those skilled in the art to identify the agents. Furthermore, the specification describes a known compound, melatonin, that will affect the circadian clock, thereby providing those skilled in the art with a reference point for comparison to determine whether an unknown agent does or does not modulate the circadian clock.

The Office Action appears to assert that the Applicants are required to provide the structure of the agents to be tested. It is respectfully submitted that the claimed invention is to a method for identifying new agents that modulate the circadian clock. The method does not require knowledge of the structure of the potential agent prior to testing it to see if it modulates a preselected biological condition controlled by the circadian clock. Accordingly, the specification provides a complete description of the steps required to perform the claimed method. The specification, therefore, adequately demonstrates that the Applicant was in possession of the

invention as claimed at the time the application was filed.

Moreover, as previously pointed out, “agent” is defined in the specification as a “chemical” or “metabolite” (specification at page 8, at paragraph [0036]). The specification further provides guidelines as to suitable boundaries for what the term “agent” encompasses at page 13, [0062]: “Agents envisioned to be used in the practice of the invention include pharmacologically active agents, therapeutic agents, biological molecules, amino acids...neuropeptides...mammalian tachykinins...agonists, antagonists and derivatives of all of the above.” Moreover, the agent modulates a preselected condition controlled by the circadian clock. Further, the specification discloses melatonin as an example of an agent that modulates a biological condition controlled by the circadian clock. Thus, the claimed method adequately defines the scope of agents to be tested with the claimed method. Accordingly, the specification adequately enables a person skilled in the art to execute the claimed method. Therefore, it is respectfully requested that this rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 8 is rejected under 35 U.S.C. § 112, second paragraph, as failing to particularly point out and distinctly claim the subject matter regarded as the invention.

Without acquiescing to the propriety of the rejection, claim 8 has been canceled without prejudice or disclaimer of the subject matter claimed therein. It is therefore respectfully submitted that the basis for this rejection is moot.

Rejection under 35 U.S.C. § 103(a)

A. Claims 1-11, 15-19, and 24-26 are rejected under 35 U.S.C. § 103(a) as obvious over Drijfhout *et al.* (J Pineal Res 20(1): 24-32, 1996), in view of Arendt (Reviews of Reprod 3: 13-22, 1998) and in further view of Sun *et al.* (PNAS 99(7): 4689-4691, 2002), and in further view of Lu *et al.* (J. Comp. Physiol. A. 173: 765-774, 1993) and Ziyal *et al.* (J. Neurosurg 88: 1050-1057, 1998).

The Office Action acknowledges that the previously provided amendments have overcome the previously cited combination of references of Drijfhout, Arendt, and Sun. The Office Action, however, alleges that the references of Ziyal and Lu disclose further surgical

methodologies that in combination with Drijhout, Arendt and Sun, render the claimed invention obvious.

Lu discloses a method for surgically removing the pineal gland. Lu does not disclose a method for monitoring the pineal gland while remaining in the subject. The method of Lu is directed to observing birds when the pineal is removed, in contrast to the claimed method of inserting a monitoring device into the pineal gland and then measuring circadian activity in the animal with the pineal gland intact. Accordingly, there is no reasonable expectation of success in obtaining the claimed invention by combining Lu with the cited references.

Ziyal discloses a surgical method for removing tumors. Ziyal discloses removing three plates of the skull without damaging the sinuses, opening the dura and removing tumors. Ziyal is not analogous art. Ziyal does not consider inserting a monitoring device into the pineal to monitor the circadian rhythm. The difference between Ziyal and the claimed invention is more than merely academic. Ziyal discloses removing three plates of the skull, separating the sinuses, opening the dura mater and removing tumors from the pineal gland. The claimed method, however, teaches a less invasive procedure that allows one skilled in the art to insert a monitoring device into the pineal while leaving the pineal gland intact, leave that monitoring device in the subject, and measure changes in the circadian rhythm.

Further, the present invention is directed to a method of accessing the pineal gland, inserting a monitoring device and then monitoring the subject's circadian rhythm. Lu and Ziyal, however, are directed to opening a skull and removing either the entire pineal or a part of the pineal containing tumors, and sewing the subject back up. Accordingly, there is no reason to combine the teachings of Lu and Ziyal with those of Drijhout, Arendt, and Sun and there is no reasonable expectation of success in obtaining the claimed invention by combining all the cited references.

As is stated in the cited reference of Drijhout, *in vivo* insertion of a monitoring device into the pineal gland has drawbacks, particularly with respect to the monitoring device damaging the sinuses (*see* Drijhout at page 937, left column, first paragraph). Ziyal does not disclose a method suitable for not damaging the sinuses and inserting a monitoring device; the skull is removed from the sinuses, and the dura is separated to allow removal of tissue. Accordingly,

Ziyal does not disclose a method that would suggest a monitoring device inserted into the pineal that would not damage the sinuses. Similarly, Lu discloses a method that allows for removal of the pineal, not a method whereby a monitoring device is inserted into the pineal gland and does not damage the sinuses.

Ziyal and Lu in effect teach away from the claimed invention in that they disclose methodologies that expose the sinuses, leaving on skilled in the art to surmise that a monitoring device would damage the sinuses, an effect Drijhout cautions against. Accordingly, one skilled in the art would not interpret Ziyal and Lu as supplying the missing features to render the claimed invention obvious. It is therefore respectfully requested that the rejection be withdrawn.

#### Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Date: **June 5, 2009**  
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Respectfully submitted,  
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